

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

JC474 U.S. PRO
10/023584



12/21/01

#2
A.Q.J
3/7/02

In re application of: Rosen et al.

Application Serial No.: Unassigned

Art Unit: Unassigned

Filed: Herewith

Examiner: Unassigned

For: **Human Vascular Endothelial Growth
Factor 2**

Attorney Docket No.: PF112P1D2

INFORMATION DISCLOSURE
STATEMENT PURSUANT TO 37 § CFR 1.56

Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

In accordance with the duty of disclosure imposed by 37 C.F.R. § 1.56 to inform the Patent and Trademark Office of all references coming to the attention of each individual associated with the filing or prosecution of the subject application, which are or may be material to the patentability of a claim of the subject application, Attorneys for Applicants hereby direct the Examiner's attention to references AA-FU listed on the attached Form PTO/SB/08A. A copy of each of references AA-FU is enclosed.

Attorneys for Applicants further wish to bring to the attention of the Examiner:

- (a) Statutory Declaration of Peter Adrian Walton Rogers executed on November 12, 2001, and exhibits PAWR-1 through PAWR-14;
- (b) Statutory Declaration of Peter Adrian Walton Rogers executed on February 16, 2000, and exhibit 1;
- (c) Statutory Declaration of Kari Alitalo executed on February 15, 2000, and exhibits 1-3;
- (d) Statutory Declaration of Francis John Ballard and exhibit 1;
- (e) Statutory Declaration of Kari Alitalo executed on September 24, 2001, and exhibits 1-2;
- (f) Statutory Declaration of John Stanley Mattick, and Exhibits JSM1-JSM4;
- (g) Statutory Declaration of Nicholas Kim Hayward, and Exhibits NKH1-2;
- (h) Statutory Declaration of Jennifer Ruth Gamble and Exhibits JRG1-3;

- (i) Statutory Declaration of Tom Rapoport and Exhibits TP1-2;
- (j) Statutory Declaration of Stuart A. Aaronson and Curriculum Vitae of Stuart A. Aaronson;
- (k) Statutory Declaration of Susan Power, Appendices 1-2 and Figure 1; and
- (l) Statutory Declaration of Gary Baxter Cox and Exhibits GBC-1 – GBC 23.

The exhibits accompanying the above-listed declarations are documents or references which were brought to the attention of the Applicants in connection with an opposition to an Australian application, that essentially corresponds to the U.S. priority application in this case. Copies of each of the above-listed Declarations and accompanying exhibits thereto, are enclosed.

The above information is presented so that the Patent and Trademark Office can determine any materiality thereof to the claimed invention. See 37 CFR §§ 1.104(a) concerning the PTO duty to consider and use any such information. It is respectfully requested that the information be considered during the prosecution of this application.

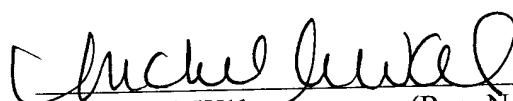
Identification of the listed reference(s) is not to be construed as an admission of any individual associated with the filing or prosecution of the subject application that such references are available as "prior art" against the subject application. Furthermore, Applicants do not waive any rights to appropriate action to establish patentability over any of the listed documents should they be applied as references against the claims of the subject application.

Applicants respectfully request that the Examiner review the listed reference(s) and that the reference(s) be made of record in the file history of the application.

Pursuant to 37 C.F.R. § 1.97(b), since this information disclosure statement is being filed before the mailing date of a first Office Action on the merits, no fee is due in connection herewith. However, should the Patent Office determine otherwise, please charge the required fee to Human Genome Sciences, Inc., deposit account no. 08-3425.

Respectfully submitted,

Dated: 12/21/01



Michele M. Wales (Reg. No. 43,975)
Attorney for Applicants

Human Genome Sciences, Inc.
9410 Key West Avenue
Rockville, Maryland 20850
Telephone: (301) 610-5772

Enclosures
MMW/AKR/lcc

Please type a plus sign (+) inside this box

PTO/SB/08 (08-00)

Approved for use through 10/31/2002. OMB 0651-0031

U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449/PTO

**INFORMATION DISCLOSURE
STATEMENT BY APPLICANT**

(use as many sheets as necessary)

Sheet

1

of

9

Complete if Known

| | |
|----------------------|-----------------------|
| Application Number | Unassigned |
| Filing Date | Concurrently Herewith |
| First Named Inventor | ROSEN, Craig |
| Group Art Unit | Unassigned |
| Examiner Name | Unassigned |

Attorney Docket Number PF112P1D2

JC474 U.S. 3584 PRO 12/21/01

| U.S. PATENT DOCUMENTS | | | | | |
|-----------------------|-----------------------|----------------------|-----------------------------------|---|--|
| Examiner Initials | Cite No. ¹ | U.S. Patent Document | | Name of Patentee or Applicant of Cited Document | Date of Publication of Cited Document MM-DD-YYYY |
| | | Number | Kind Code ² (if known) | | |
| | AA | 5,633,147 | | Meissner <i>et al.</i> | 05-27-1999 |
| | AB | 5,283,354 | | Lemischka | 02-01-1994 |
| | AC | 5,240,848 | | Keck <i>et al.</i> | 08-31-1993 |
| | AD | 5,234,908 | | Szabo <i>et al.</i> | 08-10-1993 |
| | AE | 5,194,596 | | Tischer <i>et al.</i> | 03-16-1993 |
| | FO | 5,861,301 | | Terman <i>et al.</i> | 01-19-1999 |
| | FQ | 5,840,693 | | Eriksson <i>et al.</i> | 11-24-1999 |
| | BD | 5,073,492 | | Chen <i>et al.</i> | 12-17-1991 |
| | BE | 5,219,739 | | Tischer <i>et al.</i> | 06-15-1993 |
| | BF | 5,326,695 | | Andersson <i>et al.</i> | 07-05-1994 |
| | BG | 5,607,918 | | Eriksson <i>et al.</i> | 03-04-1997 |
| | BH | 08/340011 | | | 11/1994 |
| | BI | 08/510133 | | | 08/1995 |
| | BJ | 08/585895 | | | 01/1996 |
| | BK | 08/601132 | | | 02/1996 |
| | BL | 08/671573 | | | 06/1996 |
| | BM | 60/003491 | | | 09/1995 |
| | BN | 08/554374 | | | 11/1995 |

| FOREIGN PATENT DOCUMENTS | | | | | |
|--------------------------|-----------------------|-------------------------|--------------------------------|---|--|
| Examiner Initials | Cite No. ¹ | Foreign Patent Document | | Name of Patentee or Applicant of Cited Document | Date of Publication of Cited Document MM-DD-YYYY |
| | | Office ³ | Number ⁴ (if known) | | |
| | AF | | 99/46364 | Human Genome Sciences, Inc. | 09-16-1999 |
| | AG | | 98/33917 | Ludwig Institute for Cancer Research/Univ. Helsinki Licensing Ltd. | 06-08-1998 |
| | AH | | 98/07832 | Ludwig Institute for Cancer Research/Univ. Helsinki Licensing Ltd. Oy | 02-26-1998 |

| | |
|--------------------|-----------------|
| Examiner Signature | Date Considered |
|--------------------|-----------------|

*Examiner: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

¹ Unique citation designation number. ² See attached Kinds of U.S. Patent Documents. ³ Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). ⁴ For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. ⁵ Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. ⁶ Applicant is to place a check mark here if English language Translation is attached.

Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, Washington, DC 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, Washington, DC 20231.

Please type a plus sign (+) inside this box

+

PTO/SB/08 (08-00)

Approved for use through 10/31/2002. OMB 0651-0031

U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

| | | | | | |
|---|---|----|---|--------------------------|-----------------------|
| Substitute for form 1449/PTO | | | | <i>Complete if Known</i> | |
| INFORMATION DISCLOSURE STATEMENT BY APPLICANT (use as many sheets as necessary) | | | | Application Number | Unassigned |
| | | | | Filing Date | Concurrently Herewith |
| | | | | First Named Inventor | ROSEN, Craig |
| | | | | Group Art Unit | Unassigned |
| | | | | Examiner Name | Unassigned |
| Sheet | 2 | of | 9 | Attorney Docket Number | PF112P1D2 |

| FOREIGN PATENT DOCUMENTS | | | | | |
|--------------------------------|-----------------------|-------------------------|--------------------------------------|--|---|
| Examiner Initials ¹ | Cite No. ¹ | Foreign Patent Document | | Name of Patentee or Applicant of Cited Document | Date of Publication of Cited Document MM-DD-YYYY |
| | | Office ³ | Kind Code ⁵ (if known) | | |
| | | | | | |
| | AI | | 96/39515 | Human Genome Sciences, Inc. | 12-12-1996 |
| | AJ | | 96/05856 | Human Genome Sciences, Inc. | 02-29-1996 |
| | AK | | 95/24414 | Human Genome Sciences, Inc. | 09-14-1995 |
| | AL | | 95/19985 | Human Genome Sciences, Inc. | 07-27-1995 |
| | AM | | 92/14748 | American Cyanamid Co. | 09-03-1992 |
| | FR | | 94/403464 | Human Genome Sciences, Inc. | 01-31-1996 |
| | AU | | 99/21590 | Merck & Co. | 05-06-1999 |
| | AV | | 99/08522 | Ludwig Institute for Cancer Research/Univ. Helsinki Licensing Ltd. | 02-25-1999 |
| | AW | | 98/56936 | Max-Planck-Gesellschaft Zur Forderung Der Wissenschaften E.V. | 12-17-1998 |
| | AX | | 98/49300 | Collateral Therapeutics | 11-05-1998 |
| | AY | | 98/39035 | The Wistar Institute of Anatomy & Biology | 09-11-1998 |
| | AZ | | 98/24811 | ZymoGenetics, Inc. | 06-11-1998 |
| | BB | | 98/06844 | Human Genome Sciences, Inc. | 02-19-1998 |
| | BC | | 710696 | Genentech, Inc. | 09-30-1999 |
| | BO | | 0-476983 | Bayne et al. | 03-25-1992 |
| | BP | | 0-506477 | Bayne et al. | 09-30-1992 |
| | BQ | | 97/05250 | University of Helsinki | 02-13-1997 |
| | BR | | 97/09427 | Genentech, Inc. | 03-13-1997 |
| | BS | | 97/17442 | Immunex Corporation | 05-15-1997 |

| | |
|--------------------|-----------------|
| Examiner Signature | Date Considered |
|--------------------|-----------------|

¹ Examiner: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

² Unique citation designation number. ³ See attached Kinds of U.S. Patent Documents. ⁴ Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). ⁵ For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. ⁶ Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. ⁶ Applicant is to place a check mark here if English language Translation is attached.

Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, Washington, DC 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, Washington, DC 20231.

Please type a plus sign (+) inside this box

+

PTO/SB/08 (08-00)

Approved for use through 10/31/2002. OMB 0651-0031

U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449/PTO

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(use as many sheets as necessary)

Sheet

3

of

9

Complete if Known

| | |
|----------------------|-----------------------|
| Application Number | Unassigned |
| Filing Date | Concurrently Herewith |
| First Named Inventor | ROSEN, Craig |
| Group Art Unit | Unassigned |
| Examiner Name | Unassigned |

Attorney Docket Number PF112P1D2

| OTHER REFERENCES - NON PATENT LITERATURE DOCUMENTS | | |
|--|-----------------------|---|
| Examiner Initials | Cite No. ¹ | Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published. |
| | BT | ACHEN <i>et al.</i> , "Vascular endothelial growth factor D (VEGF-D) is a ligand for the tyrosine kinases VEGF receptor-2 (Flk1) and VEGF receptor 3 (Flt4)," <i>Proc. Natl. Acad. Sci. (USA)</i> , 95(2): 548-553 (1998). ^{T2} |
| | BU | ANDERSSON <i>et al.</i> , "Assignment of interchain disulfide bonds in platelet-derived growth factor (PDGF) and evidence for agonist activity of monomeric PDGF," <i>J. Biol. Chem.</i> , 267(16): 11260-11266 (1992). |
| | BV | ALDERSON, R. F., Yourey, P. A., and Su, J. Y. (1999) Vascular endothelial cell growth factor (VEGF)-2 enhances the development of rat photoreceptor cells in vitro. <i>Keystone Symposia, Ocular Cell and Molecular Biology</i> , 202. (Abstract provided) |
| | BW | ANDERSSON W.F., "Human gene therapy," <i>Science</i> , 256:808-813 (1992). |
| | BX | Aprelikova <i>et al.</i> , "FLT4, a novel class III receptor tyrosine kinase in chromosome 5q33-pter," <i>Cancer Research</i> , 52:746-748 (1992). |
| | BY | DIGNAM <i>et al.</i> , "Balbiani ring 3 in <i>chironomus tentans</i> encodes a 185-kDa secretory protein which is synthesized throughout the fourth larval instar," <i>Gene</i> 88:133-140 (1990). |
| | BZ | FERRARA <i>et al.</i> , "Molecular and biological properties of the vascular endothelial growth factor family of proteins," <i>Endocrine Rev.</i> 13(1): 18-32 (1992). |
| | CA | FINNERTY <i>et al.</i> , "Molecular cloning of murine FLT and FLT4," <i>Oncogene</i> 8(11): 2293-2298 (1993). |
| | CB | HELDIN <i>et al.</i> , "Structure of platelet-derived growth factor: implications for functional properties," <i>Growth Factors</i> 8:245-252 (1993). |
| | CC | EICHMANN <i>et al.</i> , "Avian VEGF-C: cloning, embryonic expression pattern and stimulation of the differentiation of VEGFR2-expressing endothelial cell precursors," <i>Development</i> 125(4): 743-752 (1998). |
| | CD | PAJUSOLA <i>et al.</i> , "FLT4 receptor tyrosine kinase contains seven immunoglobulin-like loops and is expressed in multiple human tissues and cell lines," <i>Cancer Research</i> 52:5738-5743 (1992). |
| | CE | LEUNG <i>et al.</i> , "Vascular endothelial growth factor is a secreted angiogenic mitogen," <i>Science</i> 246:1306-1309 (1989). |
| | CF | BREIER <i>et al.</i> , "Expression of vascular endothelial growth factor during embryonic angiogenesis and endothelial cell differentiation," <i>Development</i> 114:521-532 (1992). |
| | CG | BELL <i>et al.</i> , "Human epidermal growth factor precursor: cDNA sequence, expression <i>in vitro</i> and gene organization," <i>Nucl. Acids Res.</i> 14(21): 8427-8446 (1986). |
| | CH | BERSE <i>et al.</i> , Vascular permeability factor (vascular endothelial growth factor) gene is expressed differentially in normal tissues, macrophages, and tumors," <i>Mol. Biol. Cell.</i> 3:211-220 (1992). |

| | |
|--------------------|-----------------|
| Examiner Signature | Date Considered |
|--------------------|-----------------|

¹Examiner: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

² Unique citation designation number. ³ Applicant is to place a check mark here if English language Translation is attached.

Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, Washington, DC 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, Washington, DC 20231.

Please type a plus sign (+) inside this box

+

PTO/SB/08 (08-00)

Approved for use through 10/31/2002. OMB 0651-0031

U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449/PTO

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(use as many sheets as necessary)

Sheet

4 of 9

Complete if Known

| | |
|----------------------|-----------------------|
| Application Number | Unassigned |
| Filing Date | Concurrently Herewith |
| First Named Inventor | ROSEN, Craig |
| Group Art Unit | Unassigned |
| Examiner Name | Unassigned |

Attorney Docket Number

PF112P1D2

OTHER REFERENCES - NON PATENT LITERATURE DOCUMENTS

| Examiner Initials | Cite No. ¹ | Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published. | T ² |
|-------------------|---|---|----------------|
| CI | BETSHOLTZ <i>et al.</i> , "cDNA sequence and chromosomal localization of human platelet-derived growth factor A-chain and its expression in tumor cell lines," <i>Nature</i> 320:695-699 (1986). | | |
| CJ | CLAFFEY <i>et al.</i> , "Vascular endothelial growth factor," <i>J. Biol. Chem.</i> 267(23): 16317-16322 (1992). <i>o</i> | | |
| CK | CORSON <i>et al.</i> , "Fibrillin binds calcium and is coded by cDNAs that reveal a multidomain structure and alternatively spliced exons at the 5' end," <i>Genomics</i> 17:476-484 (1993). <i>o</i> | | |
| CL | FERRARA <i>et al.</i> , "The vascular endothelial growth factor family of polypeptides," <i>J. Cellular Biochemistry</i> 47:211-218 (1991). | | |
| CM | GEORGE <i>et al.</i> , "Current Methods in Sequence Comparison and Analysis," Macromolecular Seq. and Syn. Selected Meth – Application (Alan R. Liss), pp. 127-149 (1988). | | |
| CN | HU <i>et al.</i> , "A novel regulatory function of proteolytically cleaved VEGF-2 for vascular endothelial smooth muscle cells," <i>FASEB J.</i> , 11:498-504 (1997). | | |
| CO | JOUKOV <i>et al.</i> , "A novel vascular endothelial growth factor, VEGF-C, is a ligand for the Flt4 (VEGFR-3) and KDR (VEGFR-2) receptor tyrosine kinases," <i>EMBO J.</i> 15(2): 290-298 (1996). <i>o</i> | | |
| CP | JOUKOV <i>et al.</i> , "Proteolytic processing regulates receptor specificity and activity of VEGF-C," <i>EMBO J.</i> 16(13): 3898-3911 (1997). | | |
| CQ | KAIPAINEN <i>et al.</i> , "The related FLT4, FLT1 and KDR receptor tyrosine kinases show distinct expression patterns in human fetal endothelial cells," <i>J. Exp. Med.</i> 178:2077-2088 (1993). | | |
| CR | KECK <i>et al.</i> , "Vascular permeability factor, an endothelial cell mitogen related to PDGF," <i>Science</i> 246: 1309 (1989). <i>o</i> | | |
| CS | KINGSLEY, D., "The TGF- β superfamily: new members, new receptors, and new genetic tests of function in different organisms," <i>Genes & Development</i> 8: 133-146 (1994). | | |
| CT | KUKK <i>et al.</i> , "VEGF-C receptor binding and pattern of expression with VEGFR-3 suggests a role in lymphatic vascular development," <i>Development</i> 122: 3829-37 (1996). | | |
| CU | LEE <i>et al.</i> , "Vascular endothelial growth factor-related protein: a ligand and specific activator of the tyrosine kinase receptor Flt4," <i>Proc. Natl. Acad. Sci. (USA)</i> , 93:1988-1992 (1996). | | |
| CV | MAGLIONE <i>et al.</i> , "Two alternative mRNAs coding for the angiogenic factor, placenta growth factor (PIGF), are transcribed from a single gene of chromosome 14," <i>Oncogene</i> 8:925-931 (1993). <i>o</i> | | |

| | |
|--------------------|-----------------|
| Examiner Signature | Date Considered |
|--------------------|-----------------|

*Examiner: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

¹ Unique citation designation number. ² Applicant is to place a check mark here if English language Translation is attached.

Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, Washington, DC 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, Washington, DC 20231.

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449/PTO

*Complete if Known***INFORMATION DISCLOSURE
STATEMENT BY APPLICANT**

(use as many sheets as necessary)

Sheet

5

of

9

Application Number

Unassigned

Filing Date

Concurrently Herewith

First Named Inventor

ROSEN, Craig

Group Art Unit

Unassigned

Examiner Name

Unassigned

Attorney Docket Number

PF112P1D2

OTHER REFERENCES - NON PATENT LITERATURE DOCUMENTS

| Examiner Initials | Cite No. ¹ | Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published. |
|-------------------|---|---|
| CW | MAGLIONE <i>et al.</i> , "Isolation of a human placenta cDNA coding for a protein related to the vascular permeability factor," <i>Proc. Natl. Acad. Sci. (USA)</i> , 88:9267-9271 (1991). | T ² |
| CX | MASSAGUE, J., "The transforming growth factor-beta family," <i>Annu. Rev. Cell Biol.</i> 6:597-641 (1990). | |
| CY | MATTHEWS <i>et al.</i> , "A receptor tyrosine kinase cDNA isolated from a population of enriched primitive hematopoietic cells and exhibiting close genetic linkage to c-kit," <i>Proc. Natl. Acad. Sci. (USA)</i> , 88:9026-9030 (1991). | |
| CZ | MILLAUER <i>et al.</i> , "High affinity VEGF binding and developmental expression suggest FLK-1 as a major regulator of vasculogenesis and angiogenesis," <i>Cell</i> 72:835-846 (1993). | |
| DA | MILLAUER <i>et al.</i> , "Glioblastoma growth inhibited <i>in vivo</i> by a dominant-negative Flk-1 mutant," <i>Nature</i> 367:576-579 (1994). | |
| DB | OLTVAI <i>et al.</i> , "Bcl-2 heterodimerizes <i>in vivo</i> with a conserved homolog, bax, that accelerates programmed cell death," <i>Cell</i> 74:609-619 (1993). | |
| DC | PAULSSON <i>et al.</i> , "The balbani ring 3 gene in <i>chironomus tentans</i> has a diverged repetitive structure split by many introns," <i>J. Mol. Biol.</i> 211:331-349 (1990). | |
| DD | PAJUSOLA <i>et al.</i> , "Two human FLT4 receptor tyrosine kinase isoforms with distinct carboxy terminal tails are produced by alternative processing of primary transcripts," <i>Oncogene</i> 8:2931-2937 (1993). | |
| DE | TISCHER <i>et al.</i> , "Vascular endothelial growth factor: A new member of the platelet-derived growth factor gene family," <i>Biochem. & Biophys. Res. Comms.</i> 165(3): 1198-1206 (1989). | |
| DF | TANAKA <i>et al.</i> , "DNA sequence encoding the amino-terminal region of the human c-src protein: implications of sequence divergence among src-type kinase oncogenes," <i>Mol. Cell Biol.</i> 7(5): 1978-1983 (1987). | |
| DG | TERMAN <i>et al.</i> , "Identification of a new endothelial cell growth factor receptor tyrosine kinase," <i>Oncogene</i> 6:1677-1683 (1991). | |
| DH | TERMAN <i>et al.</i> , "Identification of the kdr-tyrosine kinase as a receptor for vascular endothelial cell growth factor," <i>Biochem. Biophys. Res. Commun.</i> 187(3): 1579-1586 (1992). | |
| DI | TSUJIMOTO <i>et al.</i> , "Analysis of the structure, transcripts, and protein products of <i>bcl-2</i> , the gene involved in human follicular lymphoma," <i>Proc. Natl. Acad. Sci (USA)</i> , 83:5214-5218 (1986). | |
| DJ | TISCHER <i>et al.</i> , "The Human Gene for Vascular Endothelial Growth Factor," <i>J. Biol. Chem.</i> 266(18): 11947-11954 (1991). | |
| DK | FRIEDMAN, T., "A brief history of gene therapy," <i>Nat. Genetics</i> 2:93-98 (1992). | |

| | |
|--------------------|-----------------|
| Examiner Signature | Date Considered |
|--------------------|-----------------|

¹ Examiner: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

² Unique citation designation number. ³ Applicant is to place a check mark here if English language Translation is attached.

Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, Washington, DC 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, Washington, DC 20231.

Please type a plus sign (+) inside this box

+

| | | | | | |
|---|---|----|---|--------------------------|-----------------------|
| Substitute for form 1449/PTO | | | | <i>Complete if Known</i> | |
| INFORMATION DISCLOSURE STATEMENT BY APPLICANT (use as many sheets as necessary) | | | | Application Number | Unassigned |
| | | | | Filing Date | Concurrently Herewith |
| | | | | First Named Inventor | ROSEN, Craig |
| | | | | Group Art Unit | Unassigned |
| | | | | Examiner Name | Unassigned |
| Sheet | 6 | of | 9 | Attorney Docket Number | PF112P1D2 |

OTHER REFERENCES - NON PATENT LITERATURE DOCUMENTS

| Examiner Initials | Cite No. ¹ | Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published. | T ² |
|-------------------|---|---|----------------|
| DL | WILLIAMS, R.S. "Southwestern internal medicine conference: prospects for gene therapy of ischemic heart disease," <i>Am. J. Med. Sci.</i> 306(2): 129-136 (1993). | | |
| DM | HOCKEL <i>et al.</i> , "Therapeutic angiogenesis," <i>Arch. Surg.</i> 128:423-429 (1993). | | |
| DN | GUZMAN <i>et al.</i> "Efficient gene transfer into myocardium by direct injection of adenovirus vectors," <i>Circ. Res.</i> 73:1202-1207 (1993). | | |
| DO | BELLOMO <i>et al.</i> , "Mice Lacking the Vascular Endothelial Growth Factor-B Gene (Vegfb) Have Smaller Hearts, Dysfunctional Coronary Vasculature, and Impaired Recovery From Cardiac Ischemia," <i>Circ. Research</i> 89(2): e29-e35 (2000). | | |
| DP | COCKERILL <i>et al.</i> , "Angiogenesis: Models and Modulators" <i>Int'l. Rev. Cytology</i> 159:113-160 (1995). | | |
| DQ | GAMBLE <i>et al.</i> , "Regulation of In Vitro Capillary Tube Formation by Anti-Integrin Antibodies," <i>J. Cell. Bio.</i> 121(4): 931-943 (1993). | | |
| DR | GOLDSPIEL <i>et al.</i> , "Human Gene Therapy," <i>Clinical Pharmacy</i> 12: 488-505 (1993). | | |
| DS | GRIMMOND <i>et al.</i> , "Cloning and Characterization of a Novel Human Gene Related to Vascular Endothelial Growth Factor," <i>Genome Research</i> 6:124-131 (1996). | | |
| DT | HYDE <i>et al.</i> , "Correction of the ion transport defect in cystic fibrosis transgenic mice by gene therapy," <i>Nature</i> 362: 250-255. (1993). | | |
| DU | KAY <i>et al.</i> , "In Vivo Gene Therapy of Hemophilia B: Sustained Partial Correction in Factor IX-Deficient Dogs," <i>Science</i> 262:117-119 (1993). | | |
| DV | KOLODKA <i>et al.</i> , "Hepatic Gene Therapy: Efficient Retroviral-Mediated Gene Transfer into Rat Hepatocytes in Vivo," <i>Somatic Cell and Molecular Genetics</i> 19(5): 491-497 (1993). | | |
| DW | LITWIN <i>et al.</i> , "Role of Cytokines in Endothelial Cell Functions," <i>Human Cytokines</i> 101-129. | | |
| DX | SHIBUYA <i>et al.</i> , "Nucleotide sequence and expression of a novel human receptor-type tyrosine kinase gene (<i>flt</i>) closely related to the <i>fms</i> family," <i>Oncogene</i> 519-524 (1990). | | |
| DY | SILINS <i>et al.</i> , "Analysis of the Promoter Region of the Human VEGF-Related Factor Gene," <i>Biochem. Biophys. Res. Comm.</i> 230: 413-418 (1997). | | |
| DZ | STEWART <i>et al.</i> , "Insulin delivery by somatic cell gene therapy," <i>J of Mol. Endocrinology</i> 11: 335-341 (1993). | | |
| EA | TOWNSON <i>et al.</i> , "Characterization of the Murine VEGF-Related Factor Gene," <i>Biochem. & Biophys. Res. Comms.</i> 220: 922-928 (1996). | | |
| EB | WALSH <i>et al.</i> , "Gene Therapy for Human Hemoglobinopathies," <i>P.S.E.B.M.</i> 204: 289-300. | | |

| | |
|--------------------|-----------------|
| Examiner Signature | Date Considered |
|--------------------|-----------------|

¹Examiner: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

² Unique citation designation number. ³ Applicant is to place a check mark here if English language Translation is attached.

Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, Washington, DC 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, Washington, DC 20231.

Please type a plus sign (+) inside this box



Approved for use through 10/31/2002. OMB 0651-0031

U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

| | | | | | |
|---|---|----|---|--------------------------|-----------------------|
| Substitute for form 1449/PTO | | | | <i>Complete if Known</i> | |
| INFORMATION DISCLOSURE STATEMENT BY APPLICANT (use as many sheets as necessary) | | | | Application Number | Unassigned |
| | | | | Filing Date | Concurrently Herewith |
| | | | | First Named Inventor | ROSEN, Craig |
| | | | | Group Art Unit | Unassigned |
| | | | | Examiner Name | Unassigned |
| Sheet | 7 | of | 9 | Attorney Docket Number | PF112P1D2 |

OTHER REFERENCES - NON PATENT LITERATURE DOCUMENTS

| Examiner Initials | Cite No. ¹ | Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published. | T ² |
|-------------------|--|---|----------------|
| EC | YOREY, P. A., Gohari, S., Su, J. Y. and Alderson, R. F. (2000) Vascular Endothelial Cell Growth Factors Promote the In Vitro Development of Rat Photoreceptor Cells. <i>J. Neuroscience</i> , 20: 6781 - 6788. | | |
| ED | YOREY, P. A., Gohari, S., and Alderson, R. F., (1999) Vascular Endothelial Cell Growth Factor (VEGF)-2 Enhances the Development of Rat Photoreceptor Cells In Vitro. <i>Soc. Cell Biology</i> , 227. (Abstract provided) | | |
| EF | GenBank Accession No. X68203, APRELIKHOVA <i>et al.</i> , "H.sapiens mRNA for FLT4, class III receptor tyrosine kinase," November 30, 1993. | | |
| EG | GenBank Accession No. M95200, CLAFFEY <i>et al.</i> , "Mouse vascular endothelial growth factor mRNA, complete cds," April 27, 1993. | | |
| EH | GenBank Accession No. M24160, DIGNAM <i>et al.</i> , "C.tentans 185-kd secretory protein (sp185) mRNA, partial cds, clone pCt185," April 26, 1993.. | | |
| EI | GenBank Accession No. M24276, DIGNAM <i>et al.</i> , "C.tentans 140-kd secretory protein (sp140) mRNA, partial cds, clone pCt140.1," April 26, 1993. | | |
| EJ | GenBank Accession No. M24277, DIGNAM <i>et al.</i> , "C.tentans 140-kd secretory protein (sp140) mRNA, partial cds, clone pCt140.2," April 26, 1993. | | |
| EK | GenBank Accession No. D88689, FINNERTY <i>et al.</i> , "Mus musculus mRNA for flt-1, complete cds," April 14, 2000. | | |
| EL | GenBank Accession No. L07296, FINNERTY <i>et al.</i> , "Mus musculus receptor tyrosine kinase (FLT4) mRNA, complete cds," August 9, 1993. | | |
| EM | GenBank Accession No. X54936, MAGLIONE <i>et al.</i> , "H.sapiens mRNA for placenta growth factor (PIGF)," November 12, 1991. | | |
| EN | GenBank Accession No. S57152, MAGLIONE <i>et al.</i> , "Homo sapiens placenta growth factor 2 (PIGF-2) gene, partial cds," March 5, 2001. | | |
| EO | GenBank Accession No. X59397, MATTHEWS <i>et al.</i> , "Mouse Flk-1 mRNA for a tyrosine kinase receptor," November 6, 1991. | | |
| EP | GenBank Accession No. X52263, PAULSSON <i>et al.</i> , "C.tentans balbiani ring 3 (BR3) gene," December 18, 1992. | | |
| EQ | GenBank Accession No. M63971, TISCHER <i>et al.</i> , "Human vascular endothelial growth factor gene, exon 1," August , 1993. | | |
| ER | GenBank Accession No. M63972, TISCHER <i>et al.</i> , "Human vascular endothelial growth factor gene, exon 2," August 3, 1993. | | |
| ES | GenBank Accession No. M63973, TISCHER <i>et al.</i> , "Human vascular endothelial growth factor gene, exon 3," August 3, 1993. | | |
| ET | GenBank Accession No. M63974, TISCHER <i>et al.</i> , "Human vascular endothelial growth factor gene, exon 4," August 3, 1993. | | |

| | |
|--------------------|-----------------|
| Examiner Signature | Date Considered |
|--------------------|-----------------|

¹Examiner: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

² Unique citation designation number. ² Applicant is to place a check mark here if English language Translation is attached.

Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, Washington, DC 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, Washington, DC 20231.

Please type a plus sign (+) inside this box

PTO/SB/08 (08-00)

Approved for use through 10/31/2002. OMB 0651-0031
U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

| | | | | | |
|---|---|----|---|--------------------------|-----------|
| Substitute for form 1449/PTO | | | | <i>Complete if Known</i> | |
| INFORMATION DISCLOSURE STATEMENT BY APPLICANT (use as many sheets as necessary) | | | | | |
| Sheet | 8 | of | 9 | Attorney Docket Number | PF112P1D2 |

| OTHER REFERENCES - NON PATENT LITERATURE DOCUMENTS | | | | | |
|--|---|---|--|--|----------------|
| Examiner Initials | Cite No. ¹ | Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published. | | | |
| EU | GenBank Accession No. M63975, TISCHER <i>et al.</i> , "Human vascular endothelial growth factor gene, exon 5," August 3, 1993. | | | | T ² |
| EV | GenBank Accession No. M63976, TISCHER <i>et al.</i> , "Human vascular endothelial growth factor gene, exon 6," August 3, 1993. | | | | |
| EW | GenBank Accession No. M63977, TISCHER <i>et al.</i> , "Human vascular endothelial growth factor gene, exon 7," August 3, 1993. | | | | |
| EX | GenBank Accession No. M63978, TISCHER <i>et al.</i> , "Human vascular endothelial growth factor gene, exon 8," August 3, 1993. | | | | |
| EY | GenBank Accession No. M27281, KECK <i>et al.</i> , "Human vascular permeability factor mRNA, complete cds," August 3, 1993. | | | | |
| EZ | GenBank Accession No. X04571, BELL <i>et al.</i> , "Human mRNA for kidney epidermal growth factor (EGF) precursor," March 21, 1995. | | | | |
| FA | GenBank Accession No. X63556, CORSON <i>et al.</i> , "H. sapiens mRNA for fibrillin," February 17, 1997. | | | | |
| FB | GenBank Accession No. L19896, CORSON <i>et al.</i> , "Human fibrillin (FBN1) gene, 5' end including alternative exons A, B, and C, and exon M," November 8, 1994. | | | | |
| FC | GenBank Accession No. L04947, TERMAN <i>et al.</i> , "Homo sapiens (clones BT3.081.8, BT3.129.5 and BT4.169," January 6, 1995. | | | | |
| FD | GenBank Accession No. M16237, TANAKA <i>et al.</i> , "Human c-src-1 proto-oncogene, exon 2," January 13, 1995. | | | | |
| FE | GenBank Accession No. M16243, TANAKA <i>et al.</i> , "Human c-src-1 proto-oncogene, exon 3," January 13, 1995. | | | | |
| FF | GenBank Accession No. M16244, TANAKA <i>et al.</i> , "Human c-src-1 proto-oncogene, exon 4, January 13, 1995. | | | | |
| FG | GenBank Accession No. M16245, TANAKA <i>et al.</i> , "Human c-src-1 proto-oncogene, exon 5," January 13, 1995. | | | | |
| FH | GenBank Accession No. K03212, ANDERSON <i>et al.</i> , "Human c-src-1 proto-oncogene, exon 6," January 13, 1995. | | | | |
| FI | GenBank Accession No. K03213, ANDERSON <i>et al.</i> , "Human c-src-1 proto-oncogene, exon 7," January 13, 1995. | | | | |
| FJ | GenBank Accession No. K03214, ANDERSON <i>et al.</i> , "Human c-src-1 proto-oncogene, exon 8", January 13, 1995. | | | | |
| FK | GenBank Accession No. K03215, ANDERSON <i>et al.</i> , "Human c-src-1 proto-oncogene, exon 9," January 13, 1995. | | | | |
| FL | GenBank Accession No. K03216, TANAKA <i>et al.</i> , "Human c-src-1 proto-oncogene, exon 10, January 13, 1995. | | | | |

| | |
|--------------------|-----------------|
| Examiner Signature | Date Considered |
|--------------------|-----------------|

¹ Examiner: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

² Unique citation designation number. ² Applicant is to place a check mark here if English language Translation is attached.

Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, Washington, DC 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, Washington, DC 20231.

Please type a plus sign (+) inside this box

PTO/SB/08 (08-00)

Approved for use through 10/31/2002. OMB 0651-0031

U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

| | | | | | |
|---|-----------------------|----|---|--------------------------|------------|
| Substitute for form 1449/PTO | | | | <i>Complete if Known</i> | |
| INFORMATION DISCLOSURE STATEMENT BY APPLICANT (use as many sheets as necessary) | | | | Application Number | Unassigned |
| Filing Date | Concurrently Herewith | | | | |
| First Named Inventor | ROSEN, Craig | | | | |
| Group Art Unit | Unassigned | | | | |
| Examiner Name | Unassigned | | | | |
| Sheet | 9 | of | 9 | Attorney Docket Number | PF112P1D2 |

| OTHER REFERENCES - NON PATENT LITERATURE DOCUMENTS | | |
|--|--|---|
| Examiner Initials [*] | Cite No. ¹ | Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published. |
| FM | GenBank Accession No. K03217, TANAKA <i>et al.</i> , "Human c-src-1 proto-oncogene, exon 11," January 13, 1995. | T ² |
| FN | GenBank Accession No. K03218, TANAKA <i>et al.</i> , "Human c-src-1 proto-oncogene, exon 12," January 13, 1995. | |
| FO | GenBank Accession No. M13994, TSUJIMOTO <i>et al.</i> , "Human B-cell leukemia/lymphoma 2 (bcl-2) proto-oncogene mRNA encoding bcl-2-alpha protein, complete cds," October 31, 1994. | |
| FP | GenBank Accession No. M13995, TSUJIMOTO <i>et al.</i> , "Human B-cell leukemia/lymphoma 2 (bcl-2) proto-oncogene mRNA encoding bcl-3-beta protein, complete cds," October 31, 1994. | |
| FQ | GenBank Accession No. L22473, OLTVIAI <i>et al.</i> , "Human Bax alpha mRNA, complete cds," December 15, 1993. | |
| FR | GenBank Accession No. L22474, OLTVIAI <i>et al.</i> , "Human Bax beta mRNA, complete cds," December 13, 1993. | |
| FS | GenBank Accession No. AJ000185, ACHEN <i>et al.</i> , "Homo Sapiens mRNA for vascular endothelial growth factor-D," February 11, 1998. | |
| FT | International Search Report, Application No. PCT/US99/05021. | |
| FU | International Search Report, Application No. PCT/US94/05291. | |

| | |
|--------------------|-----------------|
| Examiner Signature | Date Considered |
|--------------------|-----------------|

^{*}Examiner: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

¹ Unique citation designation number. ² Applicant is to place a check mark here if English language Translation is attached.

Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, Washington, DC 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, Washington, DC 20231.



UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark Office
ASSISTANT SECRETARY AND COMMISSIONER
OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

325800-28
PF112

AUGUST 06, 1996

PTAS



100194820A

CARELLA, BYRNE, BAIN ET AL
GREGORY D. FERRARO
6 BECKER FARM ROAD
ROSELAND, NJ 07068

UNITED STATES PATENT AND TRADEMARK OFFICE
NOTICE OF RECORDATION OF ASSIGNMENT DOCUMENT

THE ENCLOSED DOCUMENT HAS BEEN RECORDED BY THE ASSIGNMENT DIVISION OF THE U.S. PATENT AND TRADEMARK OFFICE. A COMPLETE MICROFILM COPY IS AVAILABLE AT THE ASSIGNMENT SEARCH ROOM ON THE REEL AND FRAME NUMBER REFERENCED BELOW.

PLEASE REVIEW ALL INFORMATION CONTAINED ON THIS NOTICE. THE INFORMATION CONTAINED ON THIS RECORDATION NOTICE REFLECTS THE DATA PRESENT IN THE PATENT AND TRADEMARK ASSIGNMENT SYSTEM. IF YOU SHOULD FIND ANY ERRORS OR HAVE QUESTIONS CONCERNING THIS NOTICE, YOU MAY CONTACT THE EMPLOYEE WHOSE NAME APPEARS ON THIS NOTICE AT 703-308-9723. PLEASE SEND REQUEST FOR CORRECTION TO: U.S. PATENT AND TRADEMARK OFFICE, ASSIGNMENT DIVISION, BOX ASSIGNMENTS, NORTH TOWER BUILDING, SUITE 10C35, WASHINGTON, D.C. 20231.

RECORDATION DATE: 04/22/1996

REEL/FRAME: 7937/0807
NUMBER OF PAGES: 3

BRIEF: ASSIGNMENT OF ASSIGNOR'S INTEREST (SEE DOCUMENT FOR DETAILS).

ASSIGNOR:

ROSEN, CRAIG A.

DOC DATE: 02/21/1996

ASSIGNOR:

HU, JING-SHAN

DOC DATE: 02/21/1996

ASSIGNEE:

HUMAN GENOME SCIENCES, INC.
9410 KEY WEST AVENUE
ROCKVILLE, MARYLAND 20850-3338

SERIAL NUMBER: 08465968

FILING DATE: 06/06/1995
ISSUE DATE:

PATENT NUMBER:

JACQUELINE MOORE, EXAMINER
ASSIGNMENT DIVISION
OFFICE OF PUBLIC RECORDS

DATE RECEIVED: 8/9/96
DATES ENTERED: 8/9

BY: ul